Inventor Search


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=> d his

     (FILE 'HOME' ENTERED AT 09:49:49 ON 23 OCT 2003)

     FILE 'HCAPLUS' ENTERED AT 09:49:58 ON 23 OCT 2003
L1          467 S BALASUBRAMANIAN S?/AU
L2           19 S BESMAN M?/AU
L3           17 S KASHI R?/AU
L4          126 S RAMANI K?/AU
L5          622 S L1-4
L6            1 S L5 AND AHF
                SELECT RN L6 1

     FILE 'REGISTRY' ENTERED AT 09:50:56 ON 23 OCT 2003
L7           10 S E1-10

     FILE 'HCAPLUS' ENTERED AT 09:51:12 ON 23 OCT 2003
L8            1 S L6 AND L7

=> d ibib abs hitstr ind

L8   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2002:428652  HCAPLUS
DOCUMENT NUMBER:          137:10979
TITLE:                    Preparation of antihemophilic factor A-associated
                          dispersion system
INVENTOR(S):              Balasubramanian, Sathyamangalam V.;
                          Besman, Marc; Kashi, Ramesh;
                          Ramani, Karthik
PATENT ASSIGNEE(S):       The Research Foundation of State University of New
                          York, USA; Baxter Healthcare Corporation
SOURCE:                   PCT Int. Appl., 40 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2002043665      A2   20020606       WO 2001-US48201  20011130
     WO 2002043665      A3   20020711
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
             UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2002030607      A5   20020611       AU 2002-39607    20011130
     US 2002132982      A1   20020919       US 2001-997936   20011130
PRIORITY APPLN. INFO.:                   US 2000-250137P  P  20001130
                                         WO 2001-US48201  W  20011130
AB   A method for complexing AHF (antihemophilic factor A) in a
     dispersed medium, includes: providing an AHF protein, altering
     the conformational state of the AHF protein to expose
     hydrophobic domains therein, binding a stabilizer to the exposed
     hydrophobic domains, and at least partially reversing the alteration to
     assoc. at least a portion of the protein with the stabilizer.  A
     stabilized AHF dosage form, wherein >25% of the AHF
     mol., is assocd. with a stabilizer is also disclosed.  DMPC, brain
     phosphatidylserines, and cholesterol were dissolved in chloroform and the
     solvent was removed.  The multilamellar vesicles thus formed were filtered
     through a polycarbonate filter to form small unilamellar (SUVs) below 200
     nm.  The liposomes encapsulating the protein were formed by mixing the
```

liposomes in protein (AHF) contg. buffer and ethanol followed by gentle swirling .gtoreq.37.degree. to generate intermediate structures. The PEGyation of these particles were performed by adding DSPE-PEG.

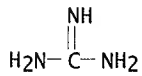
IT **113189-02-9**, Blood coagulation factor VIII
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of antihemophilic factor A-assocd. dispersion system)

RN 113189-02-9 HCAPLUS
CN Blood-coagulation factor VIII, procoagulant (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

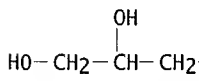
IT **50-01-1**, Guanidinium hydrochloride **56-81-5**, Glycerol, processes **57-13-6**, Urea, processes **64-17-5**, Ethanol, processes **67-56-1**, Methanol, processes **107-21-1**, Ethylene glycol, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(prepn. of antihemophilic factor A-assocd. dispersion system)

RN 50-01-1 HCAPLUS
CN Guanidine, monohydrochloride (8CI, 9CI) (CA INDEX NAME)

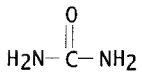


● HCl

RN 56-81-5 HCAPLUS
CN 1,2,3-Propanetriol (9CI) (CA INDEX NAME)



RN 57-13-6 HCAPLUS
CN Urea (8CI, 9CI) (CA INDEX NAME)



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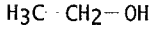
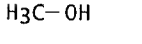
CN Ethanol (9CI) (CA INDEX NAME)



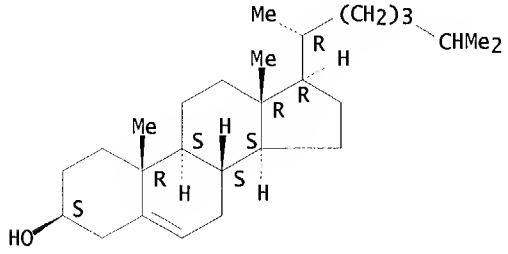
RN 67-56-1 HCAPLUS
CN Methanol (8CI, 9CI) (CA INDEX NAME)



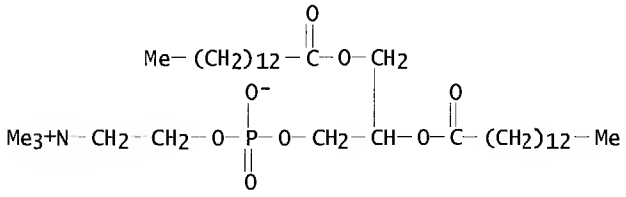
RN 107-21-1 HCAPLUS
CN 1,2-Ethanediol (9CI) (CA INDEX NAME)

IT **57-88-5**, Cholesterol, biological studies **18656-38-7**, DMPC **145035-96-7**, DSPE-PEG
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of antihemophilic factor A-assocd. dispersion system)
RN 57-88-5 HCAPLUS
CN Cholest-5-en-3-ol (3.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

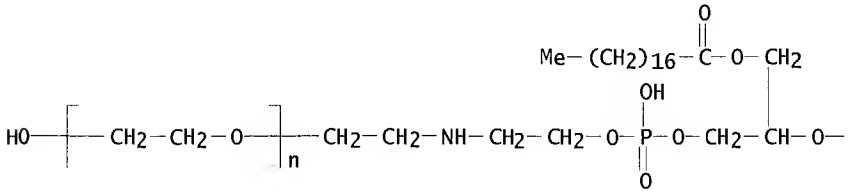


RN 18656-38-7 HCAPLUS
CN 3,5,9-Trioxa-4-phosphatricosan-1-aminium, 4-hydroxy-N,N,N-trimethyl-10-oxo-7-[(1-oxotetradecyl)oxy]-, inner salt, 4-oxide (9CI) (CA INDEX NAME)

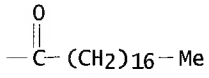


RN 145035-96-7 HCAPLUS
CN Poly(oxy-1,2-ethanediyl), .alpha.-[7-hydroxy-7-oxido-13-oxo-10-[(1-oxooctadecyl)oxy]-6,8,12-trioxa-3-aza-7-phosphatriacont-1-yl]-.omega.-hydroxy- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



IC ICM A61K

CC 63-6 (Pharmaceuticals)
ST antihemophilic factor A dispersion liposome
IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic; prepn. of antihemophilic factor A-assocd. dispersion system)
IT Drug delivery systems
(liposomes; prepn. of antihemophilic factor A-assocd. dispersion system)
IT Conformation
Solvents
Stabilizing agents
(prepn. of antihemophilic factor A-assocd. dispersion system)
IT Phosphatidylserines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of antihemophilic factor A-assocd. dispersion system)
IT Denaturation
Secondary structure
(protein; prepn. of antihemophilic factor A-assocd. dispersion system)
IT **113189-02-9**, Blood coagulation factor VIII
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of antihemophilic factor A-assocd. dispersion system)
IT **50-01-1**, Guanidinium hydrochloride **56-81-5**, Glycerol, processes **57-13-6**, Urea, processes **64-17-5**, Ethanol, processes **67-56-1**, Methanol, processes **107-21-1**, Ethylene glycol, processes
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
(prepn. of antihemophilic factor A-assocd. dispersion system)
IT **57-88-5**, Cholesterol, biological studies **18656-38-7**, DMPC **145035-96-7**, DSPE-PEG
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of antihemophilic factor A-assocd. dispersion system)

```
=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 16:15:08 ON 23 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 23 Oct 2003  VOL 139 ISS 17
FILE LAST UPDATED: 22 Oct 2003  (20031022/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
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CT = controlled terms

PFT = old, new & "used for" terms

NT = narrower term

OBI = all search fields except the abstract

CAS has 3 AHP's

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=> d que l30

L9            3 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("ANTIHEMOPHILIC C FACTOR"/CN
                  OR "ANTIHEMOPHILIC FACTOR"/CN OR "ANTIHEMOPHILIC FACTOR A"/CN
                  OR "ANTIHEMOPHILIC FACTOR B"/CN OR "ANTIHEMOPHILIC FACTOR
                  C"/CN)
L17        4464 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DENATURATION+PFT,NT/CT
L25        4656 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR AHP/OBI
L29           5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND L17
L30           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 AND (PARTICLES OR
                  DISPERSION)/TI


=> d que l37

L9            3 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("ANTIHEMOPHILIC C FACTOR"/CN
                  OR "ANTIHEMOPHILIC FACTOR"/CN OR "ANTIHEMOPHILIC FACTOR A"/CN
                  OR "ANTIHEMOPHILIC FACTOR B"/CN OR "ANTIHEMOPHILIC FACTOR
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L13      194366 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CONFORMATION+PFT,NT/CT
L19       73810 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MOLECULAR ASSOCIATION+PFT/CT
L20         689 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DENATURANTS+PFT/CT
L21        8228 SEA FILE=HCAPLUS ABB=ON  PLU=ON  STABILIZING AGENTS+PFT/CT
L22       16239 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LIPOSOMES+PFT,NT/CT
L23       86371 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DRUG DELIVERY SYSTEMS/CT
L24        7468 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23(L)LIPOSOM?
L25        4656 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR AHP/OBI
L26         111 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND L13
L32          89 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND L19
L33         189 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 OR L32
L34           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 AND (L20 OR L21)
L35           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 AND L22
L36           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 AND L24
L37           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L34 OR L35 OR L36)


=> d que l61

L9            3 SEA FILE=REGISTRY ABB=ON  PLU=ON  ("ANTIHEMOPHILIC C FACTOR"/CN
                  OR "ANTIHEMOPHILIC FACTOR"/CN OR "ANTIHEMOPHILIC FACTOR A"/CN
                  OR "ANTIHEMOPHILIC FACTOR B"/CN OR "ANTIHEMOPHILIC FACTOR
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L17        4464 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DENATURATION+PFT,NT/CT
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L22        16239 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LIPOSOMES+PFT,NT/CT
L23        86371 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DRUG DELIVERY SYSTEMS/CT
L24         7468 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L23(L)LIPOSOM?
L25         4656 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR AHP/OBI
L29            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND L17
L30            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 AND (PARTICLES OR
                 DISPERSION)/TI
L38           47 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND (L22 OR L24)
L39            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 AND DENATUR?
L40            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 AND FOLD?
L41           43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 NOT (L39 OR L40)
L42           43 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L41 NOT L30
L43        23315 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GENE THERAPY/CT
L44           32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L42 NOT L43
L61            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L44 AND (CONCENTRATED FACTOR
                 IX OR POLYMERIZABLE OR CONTAINING COAGULATION OR IX CONCENTRATE
                  OR BIOPOLYMERS OR FATTY OR INORGANIC)/TI


=> s l30 or l37 or l61

L180       11 L30 OR L37 OR L61        11 cites from HCA PLUS

=> file medline

FILE 'MEDLINE' ENTERED AT 16:15:11 ON 23 OCT 2003

 FILE LAST UPDATED: 22 OCT 2003 (20031022/UP).  FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary.  See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l81

L66        10407 SEA FILE=MEDLINE ABB=ON  PLU=ON  FACTOR VIII+NT/CT
L67          856 SEA FILE=MEDLINE ABB=ON  PLU=ON  AHP
L68        15284 SEA FILE=MEDLINE ABB=ON  PLU=ON  PROTEIN DENATURATION/CT
L69          305 SEA FILE=MEDLINE ABB=ON  PLU=ON  PROTEIN RENATURATION/CT
L70        13862 SEA FILE=MEDLINE ABB=ON  PLU=ON  PROTEIN FOLDING/CT
L71       132985 SEA FILE=MEDLINE ABB=ON  PLU=ON  PROTEIN CONFORMATION+NT/CT
L72        18865 SEA FILE=MEDLINE ABB=ON  PLU=ON  SOLVENTS/CT
L74           13 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L66 OR L67) AND L68
L75            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L66 OR L67) AND L69
L76           10 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L66 OR L67) AND L70
L77          175 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L66 OR L67) AND L71
L78            3 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L74 OR L75 OR L76 OR L77)
                 AND L72
L80         2558 SEA FILE=MEDLINE ABB=ON  PLU=ON  GUANIDINE/CT
L81            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L78 AND L80


=> d que l90

L66        10407 SEA FILE=MEDLINE ABB=ON  PLU=ON  FACTOR VIII+NT/CT
L80         2558 SEA FILE=MEDLINE ABB=ON  PLU=ON  GUANIDINE/CT
L82        62950 SEA FILE=MEDLINE ABB=ON  PLU=ON  HEAT/CT
L83          203 SEA FILE=MEDLINE ABB=ON  PLU=ON  L66 AND (L80 OR L82)
L90            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L83 AND PHOSPHATIDYL?


=> d que l109
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L66       10407 SEA FILE=MEDLINE ABB=ON  PLU=ON  FACTOR VIII+NT/CT
L106     106151 SEA FILE=MEDLINE ABB=ON  PLU=ON  TEMPERATURE/CT
L107         80 SEA FILE=MEDLINE ABB=ON  PLU=ON  L66 AND L106
L109          1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L107 AND (PHOSPHATIDYL? OR
                 LIPOSOM?)


=> d que l118

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L82       62950 SEA FILE=MEDLINE ABB=ON  PLU=ON  HEAT/CT
L106     106151 SEA FILE=MEDLINE ABB=ON  PLU=ON  TEMPERATURE/CT
L111          3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L66 AND DRUG CARRIER/CT
L112      24834 SEA FILE=MEDLINE ABB=ON  PLU=ON  DRUG STABILITY/CT
L113         59 SEA FILE=MEDLINE ABB=ON  PLU=ON  L112 AND L66
L114       2423 SEA FILE=MEDLINE ABB=ON  PLU=ON  L66(L)(TU OR PK OR PD OR
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L115         11 SEA FILE=MEDLINE ABB=ON  PLU=ON  L113 AND L114
L117          4 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L111 OR L115) AND (L106 OR
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L118          3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L117 NOT ADMINISTRATION/TI


=> d que l120

L66       10407 SEA FILE=MEDLINE ABB=ON  PLU=ON  FACTOR VIII+NT/CT
L111          3 SEA FILE=MEDLINE ABB=ON  PLU=ON  L66 AND DRUG CARRIER/CT
L120          1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L111 AND LIPOSOMES/TI


=> d que l122

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L69         305 SEA FILE=MEDLINE ABB=ON  PLU=ON  PROTEIN RENATURATION/CT
L70       13862 SEA FILE=MEDLINE ABB=ON  PLU=ON  PROTEIN FOLDING/CT
L71      132985 SEA FILE=MEDLINE ABB=ON  PLU=ON  PROTEIN CONFORMATION+NT/CT
L114       2423 SEA FILE=MEDLINE ABB=ON  PLU=ON  L66(L)(TU OR PK OR PD OR
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L121         15 SEA FILE=MEDLINE ABB=ON  PLU=ON  L114 AND (L68 OR L69 OR L70
                 OR L71)
L122          1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L121 AND HEAT DENATURATION/TI


=> s l81 or l90 or l109 or l118 or l120 or l122

L181          8 L81 OR L90 OR L109 OR L118 OR L120 OR L122
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8 cites from medline

```
=> file wpids

FILE 'WPIDS' ENTERED AT 16:15:15 ON 23 OCT 2003
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FILE LAST UPDATED:          22 OCT 2003      <20031022/UP>
MOST RECENT DERWENT UPDATE:     200368        <200368/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE


>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<
```

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://thomsonderwent.com/coverage/latestupdates/ <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER GUIDES, PLEASE VISIT:
http://thomsonderwent.com/support/userguides/ <<<

=> d que l179

L163 1062 SEA FILE=WPIDS ABB=ON PLU=ON FACTOR VIII? OR AHP OR AHF OR ANTIHEMOPHILIC(W) (FACTOR OR PROTEIN) OR ANTIHAEMOPHILIC(W) (FACTOR OR PROTEIN)
L164 20 SEA FILE=WPIDS ABB=ON PLU=ON L163 AND LIPOSOM?
L179 2 SEA FILE=WPIDS ABB=ON PLU=ON L164 AND (COMPLEXING OR DIELECTRIC)/TI

2 cites from WPI

=> dup rem l181 l180 l179 removing duplicate cites
FILE 'MEDLINE' ENTERED AT 16:15:52 ON 23 OCT 2003

FILE 'HCAPLUS' ENTERED AT 16:15:52 ON 23 OCT 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE 'WPIDS' ENTERED AT 16:15:52 ON 23 OCT 2003
COPYRIGHT (C) 2003 THOMSON DERWENT
PROCESSING COMPLETED FOR L181
PROCESSING COMPLETED FOR L180
PROCESSING COMPLETED FOR L179
L182 20 DUP REM L181 L180 L179 (1 DUPLICATE REMOVED)
ANSWERS '1-8' FROM FILE MEDLINE
ANSWERS '9-19' FROM FILE HCAPLUS
ANSWER '20' FROM FILE WPIDS

20 cites total

=> d ibib abs ind 1-8 ind = indexing terms - all of the topics covered in the full paper are listed in the indexing. The indexing can have information not covered in the abstract.

L182 ANSWER 1 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2001118088 MEDLINE
DOCUMENT NUMBER: 20582623 PubMed ID: 11148054
TITLE: Conformational origin of the aggregation of recombinant human factor VIII.
AUTHOR: Grillo A O; Edwards K L; Kashi R S; Shipley K M; Hu L; Besman M J; Middaugh C R
CORPORATE SOURCE: Department of Pharmaceutical Chemistry, University of Kansas, Lawrence, Kansas 66046 and Hyland Immuno Division, Baxter Healthcare Corporation, Duarte, California 91010, USA.
SOURCE: BIOCHEMISTRY, (2001 Jan 16) 40 (2) 586-95.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010215

AB Aggregation of proteins is a major problem in their use as drugs and is also involved in a variety of pathological diseases. In this study, biophysical techniques were employed to investigate aggregate formation in the pharmaceutically important protein, recombinant human factor VIII (rhFVIII). Recombinant human factor VIII incubated in solution at 37 degrees C formed soluble aggregates as detected by molecular sieve chromatography and dynamic light scattering. This resulted in a corresponding loss of biological activity. Fluorescence and CD spectra of

the thermally stressed rhFVIII samples did not, however, suggest significant differences in protein conformation. To identify conformational changes in rhFVIII that may be involved in rhFVIII aggregation, temperature and solutes were used to perturb the native structure of rhFVIII. Far-UV CD and FTIR studies of rhFVIII as a function of temperature revealed conformational changes corresponding to an increase in intermolecular beta-sheet content beginning at approximately 45 degrees C with significant aggregation observed above 60 degrees C. Fluorescence and DSC studies of rhFVIII also indicated conformational changes initiating between 45 and 50 degrees C. An increase in the exposure of hydrophobic surfaces was observed beginning at approximately 40 degrees C, as monitored by increased binding of the fluorescent probe, bis-anilinonaphthalene sulfonic acid (bis-ANS). Perturbation by various solutes produced several transitions prior to extensive unfolding of rhFVIII. In all cases, a common transition, characterized by an increase in the wavelength of the fluorescence emission maximum of rhFVIII from approximately 330 to 335 nm, was observed during thermal and solute perturbation of factor VIII. Moreover, this transition was correlated with an increased association of factor VIII upon incubation at 37 degrees C in the presence of various solutes. These results suggest that association of rhFVIII in solution was initiated by a small transition in the tertiary structure of the protein which produced a nucleating species that led to the formation of inactive soluble aggregates.

CT Check Tags: Human; Support, Non-U.S. Gov't

Indexing

1-Propanol
Body Temperature
Calorimetry, Differential Scanning
Chromatography, Gel
Circular Dichroism
*Factor VIII: CH, chemistry
Factor VIII: GE, genetics
Factor VIII: ME, metabolism
Guanidine
Heat
Light
Protein Conformation
Protein Folding
Protein Structure, Secondary
Protein Structure, Tertiary
*Recombinant Proteins: CH, chemistry
Recombinant Proteins: ME, metabolism
Scattering, Radiation
Solvents
Spectrometry, Fluorescence
Urea

RN 113-00-8 (Guanidine); 57-13-6 (Urea); 71-23-8 (1-Propanol); 9001-27-8 (Factor VIII)

CN 0 (Recombinant Proteins); 0 (Solvents)

L182 ANSWER 2 OF 20 MEDLINE on STN
ACCESSION NUMBER: 1998115143 MEDLINE
DOCUMENT NUMBER: 98115143 PubMed ID: 9453053
TITLE: Recombinant factor VIII SQ--inactivation kinetics in aqueous solution and the influence of disaccharides and sugar alcohols.
AUTHOR: Fatouros A; Osterberg T; Mikaelsson M
CORPORATE SOURCE: Department of Pharmaceutical Technology, Pharmacia & Upjohn AB, Stockholm, Sweden.. angelica.fatouros@eu.pnu.com
SOURCE: PHARMACEUTICAL RESEARCH, (1997 Dec) 14 (12) 1679-84. Journal code: 8406521. ISSN: 0724-8741.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199804
ENTRY DATE: Entered STN: 19980416
Last Updated on STN: 19980416

Entered Medline: 19980406

AB PURPOSE: To investigate the influence of various nonreducing disaccharides and sugar alcohols on the inactivation kinetics of recombinant factor VIII SQ (r-VIII SQ) in aqueous solution not containing albumin as a stabiliser. METHODS: The stability of r-VIII SQ was followed using measurement of activity (VIII:C) and HPLC gel filtration at different temperatures. The thermal stability was investigated using differential scanning calorimetry (DSC). RESULTS: The decline in VIII:C followed pseudo-first order kinetics. However, the Arrhenius plot was not linear for formulations without carbohydrate, demonstrating a distinct, reproducible curvature. The reaction rate at 5 degrees C was faster than expected from the Arrhenius kinetics. The energy of activation (Ea) for formulations without added carbohydrates, derived from the linear part of the Arrhenius plot, varied between 77 and 86 kJ/mole in the temperature range 20-37 degrees C. The addition of 600 mg/ml sucrose increased the Ea to 104 kJ/mole. DSC measurements showed that Tm' was 64.2 +/- 0.2 degrees C for r-VIII SQ without stabiliser. This value increased linearly with increasing concentrations of carbohydrate. This stabilising effect is most probably explained by the theory of preferential hydration. CONCLUSIONS: The inactivation kinetics of r-VIII SQ in aqueous solution without addition of carbohydrates followed pseudo-first order kinetics but the Arrhenius plot was nonlinear. Sucrose and sorbitol both had highly stabilising effects on r-VIII SQ at concentrations above 300 mg/ml. The preparation containing 600 mg/ml sucrose was stable for at least 12 months at 5 degrees C and 6 months at 25 degrees C.

CT Check Tags: Animal; Male
Calorimetry, Differential Scanning
*Disaccharides: CH, chemistry
Drug Stability
Drug Tolerance
Factor VIII: BI, biosynthesis
***Factor VIII: CH, chemistry**
Factor VIII: PD, pharmacology
Kinetics
Rabbits
Recombinant Proteins: CH, chemistry
Solutions
*Sugar Alcohols: CH, chemistry
Temperature

RN 9001-27-8 (Factor VIII)

CN 0 (Disaccharides); 0 (Recombinant Proteins); 0 (Solutions); 0 (Sugar Alcohols)

L182 ANSWER 3 OF 20 MEDLINE on STN

ACCESSION NUMBER: 94235710 MEDLINE
DOCUMENT NUMBER: 94235710 PubMed ID: 8180259
TITLE: Stability of factor VIII preparation in continuous infusion.
AUTHOR: Martinowitz U
CORPORATE SOURCE: National Hemophilia Center, Sheba Medical Center, Tel-Hashomer, Israel.
SOURCE: ANNALS OF HEMATOLOGY, (1994) 68 Suppl 3 S69-71. Journal code: 9107334. ISSN: 0939-5555.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199406
ENTRY DATE: Entered STN: 19940621
Last Updated on STN: 19990129
Entered Medline: 19940614

CT Check Tags: Comparative Study; Human
Drug Stability
***Factor VIII: AD, administration & dosage**
***Factor VIII: CH, chemistry**
Factor VIII: TU, therapeutic use
Glass

*Hemophilia A: ME, metabolism
Infusions, Intravenous
Kinetics
Plastics
Temperature
Time Factors
RN 9001-27-8 (Factor VIII)
CN 0 (Glass); 0 (Plastics)

L182 ANSWER 4 OF 20 MEDLINE on STN
ACCESSION NUMBER: 93232040 MEDLINE
DOCUMENT NUMBER: 93232040 PubMed ID: 8473326
TITLE: Membrane binding kinetics of factor VIII indicate a complex binding process.
AUTHOR: Bardelle C; Furie B; Furie B C; Gilbert G E
CORPORATE SOURCE: Center for Hemostasis and Thrombosis Research, New England Medical Center, Boston, Massachusetts.
CONTRACT NUMBER: HL42443 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1993 Apr 25) 268 (12) 8815-24.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 19930604
Last Updated on STN: 19970203
Entered Medline: 19930514

AB Factor VIII functions as a component of the tenase enzyme complex upon phospholipid membranes. Factor VIII binds to **phosphatidylserine**-containing membranes and apparently provides high affinity binding sites for factor IXa upon these membranes. We have characterized the binding kinetics of human factor VIII with **phosphatidylserine**-containing membranes and directly compared the measured properties with those of factor V. The initial phase of association was evaluated in a stopped-flow apparatus by fluorescence energy transfer from aromatic residues in the protein to dansyl-labeled **phosphatidylethanolamine** in the vesicles. Association proceeded at an apparent second-order rate of 0.12 microM-1 s-1 for extruded phospholipid vesicles and 0.42 microM-1 s-1 for sonicated vesicles under pseudo-first-order conditions in which the phospholipid concentration determined the rate. Increased temperature resulted in more rapid association, and the effect decreased in the order extruded vesicles > sonicated vesicles > extruded vesicles of dioleoylphospholipids, indicating that the structure of the phospholipid membrane contributes to the activation energy of binding. The binding of fluorescein-labeled factor VIII to membranes supported on glass microspheres (liposphères) was monitored by flow cytometry. Under conditions in which the factor VIII concentration determined the rate there was rapid initial association at 6.9 microM-1 s-1, accounting for half of the bound factor VIII, and a slower component of 0.87 microM-1 s-1, accounting for the other half. Likewise, the dissociation of factor VIII from liposphere membranes was biphasic with a faster component of 0.010 s-1 and a slower component of 0.0012 s-1. Rates of association and dissociation for factor V were similar to those for factor VIII and were biphasic. These results allow estimation of the size of the phospholipid sites that interact with factors VIII and V and suggest that both proteins bind to membranes via a multistep process in which rapid association is followed by a slower step yielding higher affinity binding.

CT Check Tags: Animal; Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Cattle
***Factor VIII: ME, metabolism**
Kinetics
*Membranes, Artificial
Phosphatidylethanolamines: ME, metabolism
Temperature

RN 9001-27-8 (Factor VIII)
CN 0 (**Phosphatidylethanolamines**)

L182 ANSWER 5 OF 20 MEDLINE on STN
ACCESSION NUMBER: 89389312 MEDLINE
DOCUMENT NUMBER: 89389312 PubMed ID: 2506696
TITLE: Severely heated therapeutic factor VIII concentrate of high specific activity.
AUTHOR: Winkelman L; Owen N E; Evans D R; Evans H; Haddon M E; Smith J K; Prince P J; Williams J D; Lane R S
CORPORATE SOURCE: Plasma Fractionation Laboratory, Churchill Hospital, Oxford, UK.
SOURCE: VOX SANGUINIS, (1989) 57 (2) 97-103.
Journal code: 0413606. ISSN: 0042-9007.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19891025

AB A new method for the manufacture of a heated factor VIII concentrate of high specific activity (2-6 IU factor VIII:C/mg protein) has been developed. Addition of heparin to cryoprecipitate extract at acid pH precipitated fibrinogen and fibronectin. Factor VIII was then recovered from the supernatant by precipitation with glycine and sodium chloride. After re-solution and desalting on Sephadex G-25, the concentrate was sterile-filtered and lyophilised. The dried product was stable to heating in the final container at 80 degrees C for 72 h. Data from 25 consecutive batches of concentrate prepared from 1,200-1,500 kg plasma pools are presented. The mean final yield of heated product was 190 IU factor VIII:C/kg plasma. The concentrate has been found to be safe and effective in clinical use.

CT Check Tags: Human
Drug Stability
Factor VIII: AD, administration & dosage
Factor VIII: AE, adverse effects
***Factor VIII: IP, isolation & purification**
Freezing
Glycine
Heat
Heparin
Precipitation
Salts: IP, isolation & purification
Sodium Chloride

RN 56-40-6 (Glycine); 7647-14-5 (Sodium Chloride); 9001-27-8 (Factor VIII); 9005-49-6 (Heparin)
CN 0 (Salts)

L182 ANSWER 6 OF 20 MEDLINE on STN
ACCESSION NUMBER: 88018701 MEDLINE
DOCUMENT NUMBER: 88018701 PubMed ID: 3116715
TITLE: The influence of pH on **heat denaturation** of anti-haemophilic cryoprecipitate.
AUTHOR: Skjonsberg O H; Gravem K; Kierulf P; Vaeret A; Godal H C
CORPORATE SOURCE: Ulleval Hospital, University Clinic, Oslo, Norway.
SOURCE: THROMBOSIS RESEARCH, (1987 Jul 15) 47 (2) 183-90.
Journal code: 0326377. ISSN: 0049-3848.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198710
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19871028

AB The influence of pH on heat denaturation of anti-haemophilic cryoprecipitate (CP) was studied by using phosphate and citrate buffers at three different pH levels for processing lyophilized, heat treated CP. The solubility and the content of FVIII:C and fibrinogen were determined following heating at 68 degrees C for 24 hours and compared to "ordinary", non-heated CP. Both the solubility and the biological activity were best preserved in the most acidic samples (pH 5.7-6.7), these batches equalled non-heated CP. At higher pH, heat treatment resulted in reduced solubility and a more pronounced loss of FVIII:C and fibrinogen. Amino acids (Syntamin 17) have previously been shown to stabilize CP during heat treatment. Some of the stabilizing effect seems to be due to a large buffering capacity, maintaining a low pH during lyophilization and heating. Raising the pH level in Syntamin-CP from 6.6 to 7.8 resulted in decreased solubility and FVIII:C content. The quality of heat treated, acidic Syntamin-CP was comparable to that of heated, acidic phosphate- and citrate-CP. We conclude that buffers used for processing heat treated CP should be of low pH, and that acidic buffers may replace Syntamin without lowering the quality of the heated product.

CT Check Tags: Human
Amino Acids: PD, pharmacology
*Blood Preservation: MT, methods
Buffers
Citrates: PD, pharmacology
*Factor VIII: AN, analysis
Factor VIII: TU, therapeutic use
Freeze Drying
Freezing
Heat
*Hydrogen-Ion Concentration
Phosphates: PD, pharmacology
Protein Denaturation: DE, drug effects
Solubility

RN 65072-01-7 (Travasol); 9001-27-8 (Factor VIII)

CN 0 (Amino Acids); 0 (Buffers); 0 (Citrates); 0 (Phosphates)

L182 ANSWER 7 OF 20 MEDLINE on STN

ACCESSION NUMBER: 89258028 MEDLINE

DOCUMENT NUMBER: 89258028 PubMed ID: 6443849

TITLE: Preparation of liposomes containing factor VIII for oral treatment of haemophilia.

AUTHOR: Kirby C J; Gregoriadis G

CORPORATE SOURCE: Division of Clinical Sciences, Clinical Research Centre, Harrow, Middlesex, England.

SOURCE: JOURNAL OF MICROENCAPSULATION, (1984 Jan-Mar) 1 (1) 33-45. Journal code: 8500513. ISSN: 0265-2048.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198906

ENTRY DATE: Entered STN: 19900306
Last Updated on STN: 19990129
Entered Medline: 19890627

AB Different types of liposomes composed of a variety of lipids have been compared for their ability to incorporate Factor VIII, with a view to attempting oral therapy of haemophilia. Reverse evaporation liposomes (REV) composed of unsaturated phospholipids, allowed adequate levels of entrapment for administration to haemophilic dogs, but failed to promote entry of Factor VIII into the vasculature, possibly due to liposome breakdown and denaturation of Factor VIII within the gastrointestinal tract. A novel technique was therefore developed which made possible high-yield entrapment of Factor VIII in much more stable liposomes based on the saturated phospholipid, distearoyl phosphatidylcholine. This new technique has a number of other important features which make it an attractive method for the incorporation of a wide range of materials into liposomes.

CT Check Tags: Animal

Administration, Oral
Dogs
Drug Carriers
*Drug Compounding: MT, methods
***Factor VIII: AD, administration & dosage**
Factor VIII: TU, therapeutic use
*Hemophilia A: DT, drug therapy
Liposomes
Phosphatidylcholines
RN 4539-70-2 (1,2-distearoyllecithin); 9001-27-8 (Factor VIII)
CN 0 (Drug Carriers); 0 (Liposomes); 0 (Phosphatidylcholines)

L182 ANSWER 8 OF 20 MEDLINE on STN
ACCESSION NUMBER: 83283329 MEDLINE
DOCUMENT NUMBER: 83283329 PubMed ID: 6411112
TITLE: The interaction between factor VIII clotting antigen (VIIICAg) and phospholipid.
AUTHOR: Yoshioka A; Peake I R; Furlong B L; Furlong R A; Giddings J C; Bloom A L
SOURCE: BRITISH JOURNAL OF HAEMATOLOGY, (1983 Sep) 55 (1) 27-36. Journal code: 0372544. ISSN: 0007-1048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198310
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19900319
Entered Medline: 19831008

AB The interaction between factor VIII clotting antigen (VIIICAg) and phospholipid (PL) was studied using a two-site solid phase immunoradiometric assay (IRMA) for VIII CAg. Incubation (2 h, 37 degrees C) of normal plasma, cryoprecipitate or factor VIII concentrate with Diagen PL (0.5 mg/unit VIIICAg) resulted in 80-90% loss of IRMA-measurable VIIICAg. No loss of factor VIII related antigen (VIIIRAg) or factor VIII clotting activity (VIIIC) was seen. Treatment of factor VIII concentrate with purified PLs showed greatest VIIICAg reduction with **phosphatidylserine**, less with **phosphatidylethanolamine**, and very little with **phosphatidylcholine**. The action of phospholipase-C (PL-C) on VIIICAg-PL complexes was investigated, with enzyme activity being monitored by thin-layer chromatography. Treatment of normal plasma, cryoprecipitate or factor VIII concentrate with PL-C (5 u/unit VIIICAg) resulted in 25%, 25% and 30% increases in VIIICAg. No increase in VIIIC or VIIIRAg was seen. Preincubation of factor VIII concentrate with PL, followed by PL-C incubation, resulted in 70-80% recovery of measurable VIIICAg. Incubation of 'activated' prothrombin complex with PL-C increased VIIICAg by 44% (Autoplex) and 80% (FEIBA), indicating VIIICAg-PL complexes are present. Incubation of factor VIII concentrate with fresh platelet lysate led to a reduction in VIIICAg (100 u/dl to 21 u/dl). In fresh platelet lysate alone low VIIICAg levels were detectable (0.71 X 10(-3) u/10(9) plt). After PL-C incubation VIIICAg levels increased to 9.8 X 10(-3) u/10(9) plt) (14-fold increase). Thus VIIICAg in platelets may be hidden by VIIICAg-PL complexes.

CT Check Tags: Human
*Antigens: ME, metabolism
Blood Platelets: ME, metabolism
Cell Extracts
Factor IX: ME, metabolism
Factor IXa
***Factor VIII: IM, immunology**
Factor VIII: ME, metabolism
Heat
Phospholipase C: PD, pharmacology
*Phospholipids: BL, blood
Radioimmunoassay
RN 9001-27-8 (Factor VIII); 9001-28-9 (Factor IX)
CN 0 (Antigens); 0 (Cell Extracts); 0 (Phospholipids); EC 3.1.4.3

(Phospholipase C); EC 3.4.21.22 (Factor IXa)

=> d ibib abs hitrn 9

L182 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:428652 HCAPLUS
DOCUMENT NUMBER: 137:10979
TITLE: Preparation of antihemophilic factor A-associated **dispersion** system
INVENTOR(S): Balasubramanian, Sathyamangalam V.; Besman, Marc; Kashi, Ramesh; Ramani, Karthik
PATENT ASSIGNEE(S): The Research Foundation of State University of New York, USA; Baxter Healthcare Corporation
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002043665	A2	20020606	WO 2001-US48201	20011130
WO 2002043665	A3	20020711		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002030607	A5	20020611	AU 2002-39607	20011130
US 2002132982	A1	20020919	US 2001-997936	20011130

PRIORITY APPLN. INFO.: US 2000-250137P P 20001130
WO 2001-US48201 W 20011130

AB A method for complexing AHF (antihemophilic factor A) in a dispersed medium, includes: providing an AHF protein, altering the conformational state of the AHF protein to expose hydrophobic domains therein, binding a stabilizer to the exposed hydrophobic domains, and at least partially reversing the alteration to assoc. at least a portion of the protein with the stabilizer. A stabilized AHF dosage form, wherein >25% of the AHF mol., is assocd. with a stabilizer is also disclosed. DMPC, brain phosphatidylserines, and cholesterol were dissolved in chloroform and the solvent was removed. The multilamellar vesicles thus formed were filtered through a polycarbonate filter to form small unilamellar (SUVs) below 200 nm. The liposomes encapsulating the protein were formed by mixing the liposomes in protein (AHF) contg. buffer and ethanol followed by gentle swirling .gtoreq.37.degree. to generate intermediate structures. The PEGyation of these particles were performed by adding DSPE-PEG.

IT **113189-02-9**, Blood coagulation factor VIII
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of antihemophilic factor A-assocd. dispersion system)

=> d ibib abs hitrn 10

L182 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:300859 HCAPLUS
DOCUMENT NUMBER: 138:309313
TITLE: Pro-micelle pharmaceutical compositions containing fatty esters
INVENTOR(S): Cho, Young W.; Lee, Keith Kwang-Ho
PATENT ASSIGNEE(S): IMI Biomed, Inc., USA

SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003030865	A1	20030417	WO 2002-US28159	20020905

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003078194	A1	20030424	US 2001-974942	20011011

PRIORITY APPLN. INFO.: US 2001-974942 A 20011011

AB The present invention provides pro-micelle compns. comprising a pharmaceutical encapsulated with a membrane of esterified C12-18 fatty acids. In the mammalian intestine, exposure to C12-18 fatty acids results in conversion of the pro-micelle to a stable micelle that effectively delivers the pharmaceutical to the systemic circulation. The present invention further provides methods of making and using such compns. A liq. orally administrable insulin-contg. formulation was prepd. as follows: Sub-mixt.-A is prepd. by dissolving the following ingredients in 95% ethanol; glycerol monooleate 2.8-3.2, lecithin 3.0-3.5, cholesterol 2.8-4.6, phosphatidic acid 0.15-0.33, and lysophosphatidylcholine 3.2-9.8 g; an antioxidant soln. was prepd. contg. Pr gallate 10-18, BHA 8-14, BHT 10-20; Sub-mixt. B was prepd. by dissolving the following ingredients in 95% EtOH; PEG-40 stearate 1.5-3.9, oleic acid, 36.5-48.9, and .alpha.-tocopherol 2.0-3.9 g, propylparaben 92-118, ascorbic acid 92-121, antioxidant 200-340, and methylparaben 580-720 mg. Sub-mixt. contained insulin (250 mg) and aprotinin, N-acetylneuraminic acid 0.9-1.8, cyclohexylurea 0.05 mg. All the above mixts. were combined and gave a microemulsion.

IT **9001-28-9**, Blood coagulation factor IX **113189-02-9**, Blood coagulation factor VIII
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pro-micelle pharmaceutical compns. contg. fatty esters)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L182 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
IC ICM A61K009-127
ICS A61K009-64; A61K009-16; A61K038-28; C07K016-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2
ST promicelle pharmaceutical insulin fatty ester
IT Drug delivery systems
(capsules; lpro-micelle pharmaceutical compns. contg. fatty esters)
IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters, C12-18; pro-micelle pharmaceutical compns. contg. fatty esters)
IT **Drug delivery systems**
(**liposomes**; pro-micelle pharmaceutical compns. contg. fatty esters)
IT Drug delivery systems
(liqs., oral; pro-micelle pharmaceutical compns. contg. fatty esters)

IT Drug delivery systems
(microemulsions; pro-micelle pharmaceutical compns. contg. fatty esters)
IT Antidiabetic agents
Drug delivery systems
Human
Surfactants
(pro-micelle pharmaceutical compns. contg. fatty esters)
IT Fatty acids, biological studies
Gelatins, biological studies
Lecithins
Lysophosphatidylcholines
Phosphatidic acids
Phospholipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pro-micelle pharmaceutical compns. contg. fatty esters)
IT 9004-10-8, Insulin, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pro-micelle pharmaceutical compns. contg. fatty esters)
IT 50-18-0, Cyclophosphamide 53-86-1, Indomethacin 54-05-7, ChloroQuine 57-22-7, Vincristine 57-47-6, Physostigmine 57-88-5, Cholesterol, biological studies 59-02-9, D-.alpha.-Tocopherol 90-34-6, PrimaQuine 129-20-4, Oxyphenbutazone 130-95-0, Quinine 147-52-4, Nafcillin 525-66-6, Propranolol 533-45-9 563-24-6, Glycerophosphatidylcholine 1403-66-3, Gentamicin **9001-28-9**, Blood coagulation factor IX 9002-72-6, Growth hormone 9007-12-9, Calcitonin 9039-53-6, Urokinase 10238-21-8, Glyburide 11096-26-7, Erythropoietin 23214-92-8, Doxorubicin 25953-19-9, Cephazolin 36322-90-4, Feldene 54910-89-3, Fluoxetine **113189-02-9**, Blood coagulation factor VIII
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pro-micelle pharmaceutical compns. contg. fatty esters)

=> d ibib abs hitrn ind 11-19

L182 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:785259 HCAPLUS
TITLE: **Inorganic**-polymer complexes for the controlled release of compounds including medicinals
INVENTOR(S): Royer, Garfield P.
PATENT ASSIGNEE(S): Royer Biomedical, Inc., USA
SOURCE: U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 935,300.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6630486	B1	20031007	US 2000-509016	20000321
US 6391336	B1	20020521	US 1997-935300	19970922
WO 9915150	A1	19990401	WO 1998-US19528	19980922
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003170307	A1	20030911	US 2003-365419	20030213

PRIORITY APPLN. INFO.: US 1997-935300 A2 19970922
WO 1998-US19528 W 19980922
US 2000-509016 A3 20000321

AB This invention relates generally to the prodn. and use of inorg.-polymer

complexes for the controlled release of compds. including medicinals. Advantageously, the inorg. used is calcium sulfate.

IT **113189-02-9**, Factor VIII
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inorg.-polymer complexes for controlled release of compds. including medicinals)

IC ICM A61K009-22
ICS A61K009-16

NCL 514303000; 514777000; 514947000; 424468000; 424499000; 424422000; 424423000; 424425000; 424426000; 424451000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 2, 15

ST inorg polymer complex calcium sulfate hemihydrate controlled release drug; sustained release formulation inorg polymer complex calcium sulfate

IT Amino acids
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic, polymers; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Peptides
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cationic; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Drug delivery systems
(controlled-release; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Albumins
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(defatted; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Toxoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Drug delivery systems
(granules; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Drug delivery systems
(injections, s.c.; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Analgesics
Anesthetics
Anti-inflammatory agents
Antibacterial agents
Antibiotics
Antidepressants
Antihypertensives
Antitumor agents
Cardiovascular agents
Complexing agents
Cylinders
Liposomes
Mammalia
Surfactants
Tranquilizers
Vaccines
(inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Ethers
Glycosaminoglycans
Lecithins
Lipids
Polynucleotides
Proteins
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Cytokines
Enkephalins
Hormones, animal
Interferons
Interleukin 2
Interleukin 4
Interleukin 6
Opioids
Tumor necrosis factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inorg.-polymer complexes for controlled release of compds. including medicinals)

IT **Drug delivery systems**
(liposomes; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Polymers
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(matrix; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Drug delivery systems
(polymer-bound; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Drug delivery systems
(prodrugs; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Drug delivery systems
(spheres; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Drug delivery systems
(sustained-release; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Drug delivery systems
(tablets; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Toxoids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tetanus; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT Drug delivery systems
(wafers; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT 9012-33-3, hexosaminidase A
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT 37377-93-8, .beta.-lipotropin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fragment; inorg.-polymer complexes for controlled release of compds. including medicinals)

IT 9004-34-6, Cellulose 9005-25-8, Starch 11138-66-2, Xanthan
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inorg.-polymer complexes for controlled release of compds. including medicinals)

IT 57-88-5, cholesterol 59-46-1, procaine 140-28-3, benzathine 1406-11-7, polymyxin 7778-18-9, calcium sulfate 9002-98-6 9003-01-4, polyacrylic acid 9003-47-8, polyvinylpyridine 9004-54-0, dextran 9004-61-9, hyaluronic acid 9005-32-7, alginic acid 9007-28-7, chondroitin sulfate 9042-14-2, dextran sulfate 10034-76-1, calcium sulfate hemihydrate 12619-70-4, cyclodextrin 22199-08-2, silver sulfadiazine 24991-23-9 25322-68-3D, alcs., esters, or ethers 25513-46-6, polyglutamic acid 25608-40-6, polyaspartic acid 26063-13-8, polyaspartic acid 26336-38-9, polyvinylamine 26913-06-4,

Poly[imino(1,2-ethanediyl)]
RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inorg.-polymer complexes for controlled release of compds. including medicinals)

IT 50-56-6, oxytocin 58-82-2, bradykinin 137-58-6, lidocaine 9001-27-8, Factor VIII 9002-01-1, streptokinase 9002-60-2, ACTH 9002-67-9, luteinizing hormone 9002-72-6, growth hormone 9002-76-0, gastrin 9002-79-3, melanocyte stimulating hormone 9007-92-5, glucagon 9034-39-3, growth hormone releasing factor 9034-40-6, LRH 9034-50-8, vasotocin 9061-61-4, nerve growth factor 11000-17-2, vasopressin 11096-26-7, erythropoietin 11128-99-7, Angiotensin II 33507-63-0, substance P 37228-64-1, glucocerebrosidase 39379-15-2, neurotensin 60118-07-2, endorphin 62229-50-9, epidermal growth factor 62683-29-8, Colony stimulating factor 64221-86-9, imipenem 74913-18-1, dynorphin 81627-83-0, M-CSF 83869-56-1, GM-CSF 85637-73-6, atrial natriuretic peptide 105857-23-6, Plasminogen activator (human tissue-type protein moiety) 109319-16-6, Factor VIII **113189-02-9**, Factor VIII 143011-72-7, G-CSF
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inorg.-polymer complexes for controlled release of compds. including medicinals)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L182 ANSWER 12 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:344044 HCAPLUS
DOCUMENT NUMBER: 132:352804
TITLE: Method for preparation of vesicles loaded with biological structures, **biopolymers** and/or oligomers
INVENTOR(S): Barenholz, Yechezkel; Bar, Lilianne K.; Diminsky, Dvorah; Baru, Moshe
PATENT ASSIGNEE(S): Israel
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6066331	A	20000523	US 1996-710576	19960813

PRIORITY APPLN. INFO.: US 1996-710576 19960813

AB A compn. useful for prepg. vesicles loaded with biol. cell-structures, biopolymers and/or -oligomers is prepd. by solubilizing amphipathic material such as a phospholipid in a polar-protic solvent miscible with water, solubilizing biol. cell-structures, biopolymers and/or -oligomers in an aq. medium, mixing the polar-protic solvent contg. the amphipathic material with the aq. medium contg. the biol. cell-structures, biopolymers and/or -oligomers, and lyophilizing the resultant mixt. to form a dry product. The dry product is hydrated in an aq. medium to form the loaded vesicles. The polar-protic solvent may be tert-butanol, and the aq. medium may contain a salt such as sodium chloride, an isoosmotic cryoprotectant such as lactose, sucrose or trehalose, or a mixt. of the salt and the cryoprotectant. A medicament for disease treatment is formed by mixing the loaded vesicles with a pharmaceutically acceptable vehicle. A mixt. of DMPC-DMPG in a molar ratio of 9:1 resp. was prepd. in tert.-butanol. An aq. HBsAg soln. such as 0.9% NaCl in a 1:1 ratio was added. The final HBsAg: phospholipids (wt./wt.) ratio was 0.0015. The soln. was frozen and dried by lyophilization. A dry powder was obtained which was reconstituted before use with double distd. sterile pyrogen-free water. Multilamellar liposomes were formed;. Loading efficiency of HBsAg was 97%. "Empty liposomes" were prepd. similarly by mixing 1 vol of aq. soln. of 0.9%. NaCl with 1 vol of lipid soln. in tertiary butanol. The extent of HBsAg exposure on the liposome surface of the sample and

liposome size was detd. The titer of antibodies which was developed was high and sufficient to protect against infection by HBV.

IT **9001-28-9**, Factor IX
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of vesicles loaded with biol. structures and biopolymers and/or oligomers)

IC ICM A61K009-127
ICS C12N011-02; G01N033-544; C07K017-02

NCL 424450000

CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 15

ST vaccine vesicle biopolymer oligomer; phospholipid vaccine vesicle biopolymer oligomer; liposome vaccine biopolymer oligomer

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hepatitis B surface; prepn. of vesicles loaded with biol. structures and biopolymers and/or oligomers)

IT **Drug delivery** systems
(**liposomes**; prepn. of vesicles loaded with biol. structures and biopolymers and/or oligomers)

IT Antitumor agents
(melanoma; prepn. of vesicles loaded with biol. structures and biopolymers and/or oligomers)

IT B cell (lymphocyte)
Cryoprotectants
Melanoma
Physiological saline solutions
Vaccines
(prepn. of vesicles loaded with biol. structures and biopolymers and/or oligomers)

IT Antibodies
Antisense RNA
Biopolymers
Complement
DNA
Enzymes, biological studies
Hormones, animal, biological studies
Oligomers
Phospholipids, biological studies
Zymogens
mRNA
tRNA
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of vesicles loaded with biol. structures and biopolymers and/or oligomers)

IT Phospholipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(soya; prepn. of vesicles loaded with biol. structures and biopolymers and/or oligomers)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surface; prepn. of vesicles loaded with biol. structures and biopolymers and/or oligomers)

IT Phospholipids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(unsatd.; prepn. of vesicles loaded with biol. structures and biopolymers and/or oligomers)

IT 75-65-0, tert-Butanol, uses
RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)
(prepn. of vesicles loaded with biol. structures and biopolymers and/or oligomers)

IT 57-50-1, Sucrose, biological studies 57-88-5, Cholesterol, biological studies 63-42-3, Lactose 99-20-7, Trehalose **9001-28-9**, Factor IX 18656-38-7, DMPC 61361-72-6, Dimyristoylphosphatidylglycerol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of vesicles loaded with biol. structures and biopolymers and/or

oligomers)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L182 ANSWER 13 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:147190 HCAPLUS
DOCUMENT NUMBER: 128:208915
TITLE: Methods for the production of protein **particles** useful for delivery of pharmacological agents
INVENTOR(S): Magdassi, Shlomo; Desai, Neil; Ferreri, Kevin; Soon-Shiong, Patrick
PATENT ASSIGNEE(S): Vivorx Pharmaceuticals, Inc., USA; Magdassi, Shlomo; Desai, Neil; Ferreri, Kevin; Soon-Shiong, Patrick
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807410	A1	19980226	WO 1997-US14661	19970819
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9739169	A1	19980306	AU 1997-39169	19970819
EP 938299	A1	19990901	EP 1997-936517	19970819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1996-23968P P 19960819
WO 1997-US14661 W 19970819

AB A method has been developed for the formation of submicron particles (nanoparticles) by heat-denaturation of proteins (such as human serum albumin) in the presence of multivalent ions (such as calcium). Also provided are novel products produced by the invention method. An appropriate concn. of multivalent ions, within a relatively narrow range of concns., induces the pptn. of protein in the form of colloidal particles, at a temp. which is well below the heat denaturation temp. of the protein (as low as 60 .degree.C for serum albumin). Temps. at which invention method operates are sufficiently low to permit incorporation of other mols. (e.g., by co-pptn.), into submicron particles according to the invention, including compds. which cannot withstand high temps. Invention methods facilitate the prodn. of protein nanoparticles and microparticles contg. various mols. (such as nucleic acids, oligonucleotides, polynucleotides, DNA, RNA, polysaccharides, ribozymes, pharmacol. active compds., and the like) useful for therapeutic, diagnostic and other purposes. The addn. of multivalent cations serves both to induce pptn., and to allow linking of neg. charged mols., such as DNA, to the neg. charged protein. Microparticles and nanoparticles were formed from albumin in the presence of CaCL2.

IT **9001-28-9**, Factor IX
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prodn. of protein particles useful for delivery of pharmacol. agents)

IC ICM A61K009-14
CC 63-6 (Pharmaceuticals)
ST protein microparticle drug delivery
IT Agglutinins and Lectins
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(galactose-binding, galaptin; prodn. of protein particles useful for delivery of pharmacol. agents)

IT Cytokines
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(macrophage-activating factor; prodn. of protein particles useful for delivery of pharmacol. agents)

IT Drug delivery systems
(microparticles; prodn. of protein particles useful for delivery of pharmacol. agents)

IT Glycopeptides
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(muramic-acid contg. diglycopeptides; prodn. of protein particles useful for delivery of pharmacol. agents)

IT Drug delivery systems
(nanoparticles; prodn. of protein particles useful for delivery of pharmacol. agents)

IT Antitumor agents
Antiviral agents
Cations
Denaturation
(prodn. of protein particles useful for delivery of pharmacol. agents)

IT Albumins, biological studies
Antibodies
Caseins, biological studies
Collagens, biological studies
DNA
Enzymes, biological studies
Fibrinogens
Fibronectins
Gelatins, biological studies
Glucocorticoids
Growth factors, animal
Hemoglobins
Immunoglobulins
Interferons
Interleukin 1
Interleukin 2
Lactalbumins
Laminins
Macrophage migration inhibitory factor
Nucleic acids
Ovalbumin
Polysaccharides, biological studies
Proteins, general, biological studies
RNA
Ribozymes
Transferrins
Transforming growth factors
Tumor necrosis factors
Vitronectin
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prodn. of protein particles useful for delivery of pharmacol. agents)

IT Macroglobulins
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(.alpha.2-; prodn. of protein particles useful for delivery of pharmacol. agents)

IT 50-56-6, Oxytocin, biological studies 665-66-7, Amantadine hydrochloride 7439-89-6D, Iron, ions, biological studies 7440-26-8D, Technetium, ions, biological studies 7440-54-2D, Gadolinium, ions, biological studies 8001-27-2, Hirudin 9000-92-4, Amylase 9001-05-2, Catalase 9001-27-8, Factor VIII **9001-28-9**, Factor IX 9001-62-1, Lipase 9001-63-2, Lysozyme 9001-75-6, Pepsin 9002-01-1, Streptokinase 9002-07-7, Trypsin 9004-07-3, Chymotrypsin 9004-10-8, Insulin,

biological studies 9007-12-9, Calcitonin 9026-93-1, Adenosine deaminase 9035-68-1, Proinsulin 9035-81-8, Antitrypsin 9039-53-6, Urokinase 9054-89-1, Superoxide dismutase 11096-26-7, Erythropoietin 14127-61-8, Calcium ion, biological studies 14701-22-5, biological studies 15158-11-9, biological studies 16397-91-4, Manganese ion (Mn2+), biological studies 22537-22-0, Magnesium ion, biological studies 22537-23-1, Aluminum ion, biological studies 22537-39-9, Strontium ion, biological studies 22541-12-4, Barium ion, biological studies 22541-53-3, biological studies 23713-49-7, Zinc ion, biological studies 30516-87-1, Zidovudine 36505-84-7, Buspirone 36791-04-5, Ribavirin 37228-64-1, Glucocerebrosidase 50924-49-7, Mizoribine 51110-01-1, Somatostatin 59277-89-3, Acyclovir 60940-34-3, Ebselen 61912-98-9, Insulin-like growth factor 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor 62683-29-8, Colony stimulating factor 70641-51-9, Edelfosine 79831-76-8, Castanospermine 93135-89-8, Methoxatone 139639-23-9, Tissue plasminogen activator 142864-19-5, Enlimomab
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prodn. of protein particles useful for delivery of pharmacol. agents)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L182 ANSWER 14 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1987:464761 HCAPLUS
DOCUMENT NUMBER: 107:64761
TITLE: Interactions of **polymerizable** phosphatidylcholine vesicles with blood components: relevance to biocompatibility
AUTHOR(S): Bonte, F.; Hsu, M. J.; Papp, A.; Wu, K.; Regen, S. L.; Juliano, R. L.
CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77225, USA
SOURCE: Biochimica et Biophysica Acta (1987), 900(1), 1-9
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The biocompatibility of polymerizable phosphatidylcholine bilayer membranes in liposome form for possible use in drug carrier systems or as surface coatings for biomaterials was studied. The SH-based polymerizable lipid 1,2-bis[1,2-(lipoyl)dodecanoyl]-sn-glycero-3-phosphocholine (dilipoyl lipid, DLL) and the methacrylic deriv.-based lipid 1,2-bis[(methacryloyloxy)dodecanoyl]-sn-glycero-3-phosphocholine (dipolymerizable lipid, DPL) bound complex mixts. of serum proteins with IgG being the most abundant bound component. DPL vesicles and anionic vesicles bound substantially more protein than other vesicle types. Polymd. DPL vesicles uniquely bound a protein of about 53 kDa which was not bound to other types of phosphatidylcholine liposomes. Likewise polymd. DPL vesicles, but not other types of phosphatidylcholine vesicles, caused a marked alteration in coagulation as measured by activated partial thromboplastin time and prothrombin time tests; this effect was due to binding and depletion of clothing factor V by the DPL polymd. vesicles. Polymd. DPL liposomes and DLL liposomes in polymd. or nonpolymd. form, were without substantial effect on platelet aggregation. However, DPL nonpolymd. vesicles, while not causing aggregation, did impair ADP-induced aggregation of platelets. Thus, SH based polymerizable lipids of the DLL type may be very suitable for in vivo use in the contexts of drug delivery systems or biomaterials development. Methacryloyl-based lipids of the DPL type seem to display interactions with the hemostatic process which militate against their in vivo utilization.
IT **113189-02-9**
RL: BIOL (Biological study)
(polymerizable phosphatidylcholines effect on)
CC 63-5 (Pharmaceuticals)
Section cross-reference(s): 1
ST phosphatidylcholine polymn biocompatibility; biomaterial coating polymn phosphatidylcholine; liposome drug carrier biomaterial coating
IT Blood platelet

(aggregation of, on polymerizable phosphatidylcholines)
IT Phosphatidylcholines, biological studies
RL: BIOL (Biological study)
(liposomes contg. polymerizable., blood compatibility of, for drug carriers and biomaterial coatings)
IT Proteins, biological studies
RL: BIOL (Biological study)
(of blood, polymerizable phosphatidylcholine binding by)
IT Haptoglobins
RL: BIOL (Biological study)
(polymerizable phosphatidylcholine binding by)
IT Prosthetic materials and Prosthetics
(polymerizable phosphatidylcholine coatings for, blood compatibility of)
IT Albumins, biological studies
Fibrinogens
Macroglobulins
Transferrins
RL: BIOL (Biological study)
(polymerizable phosphatidylcholines binding by)
IT **Liposome**
(polymerizable phosphatidylcholines, blood compatibility of, for biomaterial coating)
IT Lipoproteins
RL: BIOL (Biological study)
(E, polymerizable phosphatidylcholines binding by)
IT Pharmaceutical dosage forms
(liposomes, polymerizable phosphatidylcholine vehicles for, blood compatibility of)
IT Globulins, biological studies
RL: BIOL (Biological study)
(.gamma.-, polymerizable phosphatidylcholines binding by)
IT 80294-17-3 104807-08-1
RL: BIOL (Biological study)
(blood compatibility of liposomes contg., for drug carriers and biomaterial coatings)
IT 9001-24-5, Blood coagulation factor V 9001-25-6, Blood coagulation factor VII **113189-02-9**
RL: BIOL (Biological study)
(polymerizable phosphatidylcholines effect on)
IT 79605-84-8 104778-79-2
RL: BIOL (Biological study)
(polymerizable, biocompatibility of liposomes contg., for drug carriers and biomaterial coatings)

L182 ANSWER 15 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1984:588884 HCAPLUS
DOCUMENT NUMBER: 101:188884
TITLE: Behavior of blood proteins at the interface with procoagulant phospholipids and anticoagulant heparin or polymeric biomaterials: a fluorescence study
AUTHOR(S): Dachary, J.; Dulos, E.; Faucon, J. F.; Boisseau, M. R.; Dufourcq, J.
CORPORATE SOURCE: Cent. Rech. Paul Pascal, Domaine Univ., Talence, 33405, Fr.
SOURCE: Colloids and Surfaces (1984), 10, 91-9
CODEN: COSUD3; ISSN: 0166-6622
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Changes in the fluorescence of factors IX and II in the presence of Ca at procoagulant phospholipid interfaces suggest a conformational change of the proteins upon binding. Shifts of transition temp. of phosphatidylcholine-phosphatidylserine mixts. towards those of the pure lecithin component when Ca and coagulation factors are added suggest that lateral phase sepn. does exist. The higher resonance-energy transfer efficiency with charged pyrene-labeled phospholipids leads to the conclusion that within the membrane, factor II and IX binding sites are

domains of phosphatidylserine. Ca-independent phospholipid binding, selective for phosphatidylserine, is well documented and is proposed to be mediated by electrostatic forces between the arginine and lysine residues of the proteins and the neg. charges of the phosphatidylserine. The binding of heparin or the synthetic anticoagulant polystyrene (bearing SO32- and glutamic acid groups) with antithrombin or thrombin induces different fluorescence changes in these proteins which cause local changes in the tryptophan residues of the proteins upon binding. The interaction of heparin with various mixts. of thrombin and antithrombin indicates that heparin does not modify the structure of the preformed thrombin-antithrombin complex. as far as can be seen by spectrofluorimetry.

IT **9001-28-9**
RL: BIOL (Biological study)
(procoagulant phospholipids interaction with human, protein conformation in relation to)

CC 13-5 (Mammalian Biochemistry)
Section cross-reference(s): 7

ST phospholipid coagulation factor interaction; heparin coagulation factor interaction; anticoagulant coagulation factor interaction; polymer anticoagulant coagulation factor interaction; blood clotting factor phospholipid interaction

IT Phosphatidylserines
RL: BIOL (Biological study)
(liposomes contg. phosphatidylcholine and, blood-coagulation factors II and IX of human interaction with, protein conformation in relation to)

IT Phosphatidylcholines, biological studies
RL: BIOL (Biological study)
(liposomes contg. phosphatidylserine and, blood-coagulation factors II and IX of human interaction with, protein conformation in relation to)

IT **Conformation and Conformers**
(of blood-coagulation factors II and IX of human, procoagulant phospholipid binding effect on, antithrombin and thrombin interactions with heparin in relation to)

IT **Molecular association**
(of blood-coagulation factors II and IX of humans with procoagulant phospholipids)

IT Phase transition
(of phosphatidylcholine and phosphatidylserine, binding of blood-coagulation factors II and IX of human effect on)

IT **Liposome**
(phosphatidylcholine-phosphatidylserine, blood-coagulation factors II and IX of human binding to)

IT Phospholipids
RL: BIOL (Biological study)
(procoagulant, blood-coagulation factors II and IX of human binding to, protein conformation response to)

IT 9000-94-6
RL: BIOL (Biological study)
(III, heparin interaction with, of human, protein conformation in relation to)

IT 9005-49-6, biological studies
RL: BIOL (Biological study)
(antithrombin III and thrombin III of human interaction with, protein conformation in relation to)

IT 56-86-0D, polymer with polystyrene deriv. 9003-53-6D, deriv., polymer with glutamic acid
RL: BIOL (Biological study)
(antithrombin III and thrombin of human interaction with, protein conformation in relation to)

IT 7440-70-2, biological studies
RL: BIOL (Biological study)
(blood-coagulation factors II and IX of human interaction with procoagulant phospholipids in presence of)

IT 9002-04-4
RL: BIOL (Biological study)
(heparin interaction with, of human, protein conformation in relation

to)
IT 3036-82-6
RL: BIOL (Biological study)
(liposomes contg. dimyristoylphosphatidylcholine and, blood-coagulation factors II and IX of human interaction with, protein conformation in relation to)
IT 18656-38-7
RL: BIOL (Biological study)
(liposomes contg. dipalmitoylphosphatidylserine and, blood-coagulation factors II and IX of human interaction with, protein conformation in relation to)
IT 2644-64-6
RL: BIOL (Biological study)
(liposomes contg. phosphatidylserine and, blood-coagulation factor II of human interaction with, protein conformation in relation to)
IT 9001-26-7 **9001-28-9**
RL: BIOL (Biological study)
(procoagulant phospholipids interaction with human, protein conformation in relation to)

L182 ANSWER 16 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1983:510607 HCAPLUS
DOCUMENT NUMBER: 99:110607
TITLE: Basic studies on oral and rectal administration of factor **IX concentrate** preparation
AUTHOR(S): Sakuragawa, Nobuo; Takahashi, Kaoru; Horikoshi, Isamu; Ueno, Masaharu
CORPORATE SOURCE: Cent. Clin. Lab., Toyama Med. Pharm. Univ., Toyama, Japan
SOURCE: Nippon Ketsueki Gakkai Zasshi (1983), 46(1), 190-6
CODEN: NKGZAE; ISSN: 0001-5806
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The stability of a factor IX [**9001-28-9**] conc. and its enclosure in liposomes for oral and rectal administration were investigated. Factor IX was stable at pH 8.0, and also stable at pH 7.0 by the addn. of aprotinin [9087-70-1]. Factor IX conc. itself contains activated coagulation factors, which convert prothrombin into thrombin spontaneously. This prepn. was stabilized by the addn. of aprotinin. The trapping rate of aprotinin by liposome was as low as 5.6%. The coagulation factors (100 and 400 units of factor IX) could be transferred into the blood efficiently with either oral administration or rectal application in dogs.
IT **9001-28-9**
RL: BIOL (Biological study)
(conc., stability and liposome encapsulation of, for oral and rectal administration)
CC 63-5 (Pharmaceuticals)
ST factor IX conc oral rectal; aprotinin factor IX conc; liposome factor IX conc
IT Digestive tract
(factor IX absorption by)
IT **Liposome**
(factor IX conc. encapsulation by)
IT Intestine, metabolism
(rectum, factor IX absorption by)
IT **9001-28-9**
RL: BIOL (Biological study)
(conc., stability and liposome encapsulation of, for oral and rectal administration)
IT 9087-70-1
RL: BIOL (Biological study)
(factor IX conc. stability by)

L182 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1982:588254 HCAPLUS
DOCUMENT NUMBER: 97:188254

TITLE: Pharmaceutical composition for oral administration **containing coagulation** factor VIII or IX
INVENTOR(S): Horikoshi, Isamu; Sakuragawa, Nobuo; Ueno, Masaharu; Takahashi, Kaoru
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd. , Japan
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4348384	A	19820907	US 1981-309269	19811007
JP 57070814	A2	19820501	JP 1980-144508	19801017
JP 03000366	B4	19910107		
JP 57179122	A2	19821104	JP 1981-65685	19810428
JP 03000851	B4	19910109		

PRIORITY APPLN. INFO.: JP 1980-144508 19801017
JP 1981-65685 19810428

AB An oral prepn. for the treatment of hemophilia A or B consists of blood coagulation factor VIII [9001-27-8] or factor IX [**9001-28-9**] and a protease inhibitor incorporated in liposomes and (or) encapsulated in enteric capsules. The product provides for absorption of the coagulation factor from the intestinal tract without significant decompn. Thus, liposomes were prepd. from egg yolk lecithin contg. 5% alc. phosphatidic acid and a pH 7 phosphate buffer soln. of factor VIII (3000 units); aprotinin [9087-70-1] was added and the liposome suspension was washed with NaCl soln., cooled, centrifuged, and the liposomes were dried. Intestinal capsules were packed with 10 mL liposomes contg. 1000 units of factor VIII and 17,000 units aprotinin to give 50 units of factor VIII/capsule.

IT **9001-28-9**
RL: BIOL (Biological study)
(enteric-encapsulated liposomes contg. aprotinin and, for oral hemophilia treatment)

IC A61K035-14
NCL 424101000
CC 63-3 (Pharmaceuticals)
ST blood coagulation factor liposome oral; hemophilia oral coagulation factor

IT **Liposome**
(blood coagulation factors VIII and IX incorporated in, for oral hemophilia treatment)

IT Phosphatidic acids
RL: BIOL (Biological study)
(calcium salts, liposomes contg. egg yolk lecithin and, for enteric-encapsulated blood coagulation factors, for hemophilia treatment)

IT Lecithins
RL: BIOL (Biological study)
(egg yolk, enteric-coated liposomes contg. phosphatidic acids and, for blood coagulation factors)

IT Intestine, metabolism
(liposome-incorporated blood coagulation factors VIII and IX absorption by, from capsules)

IT Phosphatidic acids
RL: BIOL (Biological study)
(liposomes contg. egg yolk lecithin and, for enteric-encapsulated blood coagulation factors, for hemophilia treatment)

IT Hemophilia
(A, treatment of, with enteric-encapsulated liposomes contg. blood coagulation factors VIII and IX and protease inhibitor)

IT Hemophilia
(B, treatment of, with enteric-encapsulated liposomes contg. blood coagulation factors VIII and IX and protease inhibitor)

IT 9001-27-8 **9001-28-9**
RL: BIOL (Biological study)
(enteric-encapsulated liposomes contg. aprotinin and, for oral hemophilia treatment)
IT 9087-70-1
RL: BIOL (Biological study)
(enteric-encapsulated liposomes contg. blood coagulation factors VIII or IX and, for hemophilia treatment)

L182 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1982:550625 HCAPLUS
DOCUMENT NUMBER: 97:150625
TITLE: Oral and rectal administration to beagle dogs of factor **IX concentrates**
AUTHOR(S): Sakuragawa, Nobuo; Takahashi, Kaoru; Horikoshi, Isamu; Ueno, Masaharu
CORPORATE SOURCE: Cent. Lab., Toyama Med. Pharm. Univ., Toyama, Japan
SOURCE: Saishin Igaku (1982), 37(7), 1414-18
CODEN: SAIGAK; ISSN: 0370-8241
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB factor IX [**9001-28-9**] Was stable at pH 8.0, and addn. of aprotinin [9087-70-1] stabilized it even at pH 7.0. Factor IV was sealed into liposomes more efficiently on addn. of Ca and stearylamine [124-30-1].
IT **9001-28-9**
RL: BIOL (Biological study)
(concs., stabilization and liposome encapsulation of)
CC 63-3 (Pharmaceuticals)
ST factor IX conc; liposome factor IX conc; aprotinin factor IX conc
IT **Liposome**
(blood-coagulation factor IX encapsulation by)
IT 9087-70-1
RL: BIOL (Biological study)
(blood coagulation factor IX conc. stabilization by)
IT 7440-70-2, biological studies
RL: BIOL (Biological study)
(blood coagulation factor IX encapsulation in liposomes in presence of)
IT 124-30-1
RL: BIOL (Biological study)
(blood coagulation factor IX encapsulation in liposomes with)
IT **9001-28-9**
RL: BIOL (Biological study)
(concs., stabilization and liposome encapsulation of)

L182 ANSWER 19 OF 20 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1982:223071 HCAPLUS
DOCUMENT NUMBER: 96:223071
TITLE: Studies on oral administration of **concentrated factor IX** preparation
AUTHOR(S): Ueno, Masaharu; Horikoshi, Isamu; Takahashi, Kaoru; Sakuragawa, Nobuo
CORPORATE SOURCE: Dep. Hosp. Pharm., Toyama Med. Pharm. Univ., Toyama, 930-01, Japan
SOURCE: Yakugaku Zasshi (1982), 102(2), 202-6
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB blood-coagulation factor IX [**9001-28-9**] Was stable at 4-25.degree. in mildly alk. solns. and was effectively encapsulated in liposome prepns. contg. 5% stearylamine or 0.02 M Ca2+; oral administration of the liposome-entrapped factor IX shortened clotting time in dogs. The transformation of prothrombin [9001-26-7] into thrombin [9002-04-4] was inhibited by adding phosphatidylcholines (250 mg) or 50,000 units aprotinin [9004-04-0]. The intestinal absorption of factor II, VII [9001-25-6], IX, and X [9001-29-0] is described.
IT **9001-28-9**

RL: BIOL (Biological study)
(liposome-entrapped, oral administration of)
CC 63-3 (Pharmaceuticals)
ST factor IX liposome oral prepn
IT **Liposome**
(blood-coagulation factor IX encapsulated by)
IT Phosphatidylcholines, biological studies
RL: BIOL (Biological study)
(prothrombin transformation into thrombin inhibition by)
IT 9002-04-4
RL: FORM (Formation, nonpreparative)
(formation of, from prothrombins, inhibitors of)
IT 9001-25-6 9001-29-0
RL: PROC (Process)
(intestine absorption of)
IT **9001-28-9**
RL: BIOL (Biological study)
(liposome-entrapped, oral administration of)
IT 9087-70-1
RL: BIOL (Biological study)
(prothrombin transformation into thrombin inhibition by)
IT 9001-26-7
RL: PROC (Process)
(transformation of, into thrombin, inhibitors for)

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L182 ANSWER 20 OF 20 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 1989-220140 [30] WPIDS
CROSS REFERENCE: 1987-095635 [14]; 1990-382605 [51]
DOC. NO. NON-CPI: N1989-167754
DOC. NO. CPI: C1989-097845
TITLE: Heat processing system - esp. useful for sterilising blood plasma prods., subjects prods. to microwave energy after **dielectric** enhancing additive addn..
DERWENT CLASS: D22 P34 S05
PATENT ASSIGNEE(S): (CHAR-I) CHARM S E
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 4839142	A	19890613	(198930)*		7

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 4839142	A	US 1987-71733	19870708

PRIORITY APPLN. INFO: US 1985-782019 19850930; US 1987-71733 19870708
AN 1989-220140 [30] WPIDS
CR 1987-095635 [14]; 1990-382605 [51]
AB US 4839142 A UPAB: 19940307
Treatment process for heat-sensitive biological fluid (I) comprises preoteinaceous material and a pathoqenic organism is claimed. The method comprises (a) rapidly heatinq (I) with a dielectric constant of more than 90 at a rate of more than 25 deg.C per sec., to a preselected temp. using microwave heating enerqy; (b) holding (I) at the preselected temp. for up to about 2 secs.; (c) rapidly cooling to a preselected lower temp; and (d) circulating the heated (I) while rapidly heating, holdinq and rapidly cooling.
The heating, holding and cooling time periods are sufficiently short and the preselected heating temp. and the lower temp. are sufficient not

to effect the desirable properties of the proteinaceous material but sufficient for at least the partial destruction of the pathogenic organism. Also claimed is a method for heating blood plasma or serum to destroy an infectious agent which comprises adding a dielectric salt to increase the dielectric constant to 90-300, then rapidly heating to at least 60 deg.C for less than 0.1 sec. by microwave heating energy to destroy the agent without altering albumin or blood clotting Factors VIII and IX of the blood plasma or serum. The high temp., short time heat process system is also claimed.

USE/ADVANTAGE - The method may be used to sterilise a wide variety of bological fluids, such as microbial media, tissue culture media, suspensions which cannot be sterilised employing ultrafiltration, such as liposomes or collagens, vaccines, mother's milk, fermentation media and cell culture media. The method may also be used to sterilise blood plasma to selectively destroy agents, such as viruses (e.g. hepatitis and AIDS), and microplasma. The method may also be used to sterilise blood plasma to selectively destroy agents, such as viruses (e.g. hepatptis and AIDS) and microplasma. The method permits continuous and rapid heating of (I) and is useful for small scale laboratory prodn. . Dwg.1/1